Exelixis Reports Encouraging Phase 1 Data for XL184 at EORTC-NCI-AACR Symposium

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Preliminary Results Show 55% Response Rate and 84% Disease Control Rate in Expanded Population of Patients with Medullary Thyroid Cancer

GENEVA--(BUSINESS WIRE)--

Exelixis, Inc. (Nasdaq:EXEL) today reported encouraging new data from an ongoing phase 1 clinical trial of XL184, a novel small molecule inhibitor of MET, VEGFR2, and RET, in patients with advanced malignancies. A total of 84 patients have been treated in the study, including 36 with medullary thyroid cancer (MTC). The results showed a disease control rate of 84% and a response rate of 55% in evaluable patients with MTC. Razelle Kurzrock, MD, Professor of Medicine and Chief of the Section on Cytokines in the Department of Bioimmunotherapy at the University of Texas M.D. Anderson Cancer Center in Houston, Texas, and Steven I. Sherman, MD, Chair and Professor, Department of Endocrine Neoplasia and Hormonal Disorders, University of Texas M.D. Anderson Cancer Center, lead investigators in the trial, presented the new data in a poster session (Abstract #379) at the EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, which is being held October 21-24 in Geneva, Switzerland. The poster will be available today on the Exelixis web site. Based on earlier positive data in this ongoing phase 1 clinical trial, Exelixis initiated a phase 3 trial of XL184 in MTC in July of this year. A phase1/2 trial in non-small cell lung cancer and a phase 2 trial in glioblastoma multiforme are also ongoing with XL184.

"Patients with medullary thyroid cancer are a highly underserved population as there are no approved and effective therapies available. Targeted therapeutics, such as dual inhibitors of RET and VEGFR2, are the first compounds showing activity in this disease. The phase 1 results reported today for XL184, the first such molecule in this class to also inhibit the MET receptor tyrosine kinase, are remarkable in terms of the high frequency of responses, how rapidly they occur, and the observation of responses in patients who previously progressed on other tyrosine kinase inhibitors," said Steven I. Sherman, MD, Chair and Professor, Department of Endocrine Neoplasia and Hormonal Disorders, University of Texas M.D. Anderson Cancer Center. "I'm looking forward to the progress of the phase 3 trial of XL184 in this indication and believe that studies like this will advance the care of patients with medullary thyroid cancer."

In the ongoing phase 1 trial, the maximum tolerated dose (MTD) for XL184 had previously been determined to be 175 mg/day given orally once-daily. Based on initial signs of clinical activity in a number of patients with MTC during the dose-escalation phase, the trial had been expanded to treat additional patients with MTC at the MTD. In the expanded trial, 22 MTC patients had received treatment with XL184 for at least 3 months and were evaluable for tumor response. In these patients, the data presented at the EORTC-NCI-AACR meeting showed a disease control rate (percentage of patients with partial responses or prolonged stable disease greater than3 months) of 84%, with 55% of the response-evaluable MTC patients experiencing partial responses as determined by RECIST criteria. Four of these partial responses were seen after only 28 days of dosing. With only two exceptions, the evaluated MTC patients had reductions in the MTC-associated plasma marker calcitonin.

"We believe the results for XL184 are impressive, and strongly support our recent initiation of a pivotal trial in patients with MTC. Based on the current data, we believe that XL184 has a strong potential to become the best-in-class therapy in this indication," said Michael M. Morrissey, PhD, President of Research and Development at Exelixis. "Given the potent activity of XL184 against MET, RET, and VEGFR2, and the observed long-lasting disease stabilization in a variety of tumor types in this phase 1 trial, we will continue to explore the compound's utility as a single agent, or in combination with other therapies, in tumor types such as lung cancer, glioblastoma, and potentially many others."

In an ongoing analysis of the RET mutational status of MTC patients, all patients with a known RET mutation were found to show clinical improvement in response to XL184. However, most patients without detectable RET mutations also showed clinical improvement, suggesting that the activity of XL184 in MTC may be independent of RET mutational status. Only one MTC patient showed disease progression by RECIST criteria after at least one post-baseline radiographic evaluation, and this patient was determined to have an activating BRAF mutation.

XL184 was generally well tolerated at the MTD of 175 mg QD (capsule). Adverse events related to the study drug included diarrhea, nausea, fatigue, mucositis, anorexia, elevation of liver enzymes, hypertension, vomiting, hair hypopigmentation, and palmar-plantar erythema. Dose-limiting toxicities included palmar-plantar erythema, elevation of liver enzymes, lipase elevation, and mucositis.

Pharmacokinetic analyses indicated that the half-life of XL184 is approximately 100 hours (range 59-136 hours), with exposure at the MTD exceeding that required for efficacy in preclinical models. Pharmacodynamic analyses demonstrated statistically significant changes at the MTD in plasma markers including VEGF-A, placental growth factor (PlGF), and soluble VEGFR2, similar to the effects of other anti-angiogenic agents, and consistent with the anti-VEGFR activity of XL184. In addition, increases in soluble MET were measured in 4 of 7 patients at the MTD who were analyzed for this endpoint.

Most of the MTC patients in the trial had previously failed other treatments, including tyrosine kinase inhibitors with anti-RET activity (e.g., vandetanib, sorafenib, and motesanib), chemotherapeutics, immunotherapy, radioactive iodine, and radiotherapy.

About XL184

XL184 inhibits MET, RET, and VEGFR2, which are key drivers of tumor growth, metastasis, survival, and angiogenesis. In pharmacodynamic studies

in mice, oral administration of XL184 resulted in balanced and durable inhibition of these targets. The compound has also shown activity against common mutant forms of RET and MET. XL184 has exhibited dose-dependent tumor growth inhibition and tumor regression in a variety of preclinical tumor models, including breast cancer, colon cancer, MTC, non-small cell lung cancer, and glioblastoma.

About Medullary Thyroid Cancer

The American Cancer Society estimates that MTC accounts for 5% of all thyroid cancers. MTC occurs in sporadic and inherited forms (approximately 80% and 20% of MTC, respectively), and is frequently associated with genetic activation of RET. The inherited form usually appears at a younger age, while dietary iodine deficiency and radiation exposure are risk factors for the sporadic form. MTC may metastasize to lymph nodes or other organs before it is ever diagnosed. Additionally, MTC does not take up radioactive iodine, which is commonly used to treat other types of thyroid cancers and to diagnose metastases. As a result, MTC is more difficult to treat than other thyroid cancers. There are no approved therapies for MTC; however, common treatments for MTC include surgery to remove malignant tissue, radiation therapy, and chemotherapy, all of which are associated with potential side effects, some of which may be long-term.

About Exelixis

Exelixis, Inc. is a development-stage biotechnology company dedicated to the discovery and development of novel small molecule therapeutics for the treatment of cancer and other serious diseases. The company is leveraging its fully integrated drug discovery platform to fuel the growth of its development pipeline, which is primarily focused on cancer. Currently, Exelixis' broad product pipeline includes investigational compounds in phase 3, phase 2, and phase 1 clinical development. Exelixis has established strategic corporate alliances with major pharmaceutical and biotechnology companies, including GlaxoSmithKline, Bristol-Myers Squibb, Genentech, Wyeth Pharmaceuticals, and Daiichi-Sankyo. For more information, please visit the company's web site at www.exelixis.com.

Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements related to the impact of XL184 studies on the advancement of care for patients with MTC; the potential of XL184 to become the best-in-class therapy in the MTC indication; and the future development path for XL184. Words such as "believe," "potential," "will," "continue," and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Exelixis' current plans, assumptions, beliefs, and expectations. Forward-looking statements involve risks and uncertainties. Exelixis' actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation: the potential failure of XL184 to demonstrate safety and efficacy in clinical testing; the therapeutic and commercial value of XL184; the ability to conduct XL184 clinical trials sufficient to achieve a positive completion; and the uncertainty of the U.S. Food and Drug Administration approval process. These and other risk factors are discussed under "Risk Factors" and elsewhere in Exelixis' quarterly report on Form 10-Q for the quarter ended June 27, 2008, and other filings with the Securities and Exchange Commission. Exelixis expressly disclaims any duty, obligation, or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in Exelixis' expectations with regard thereto or any change in events, conditions, or circumstances on which any such statements are based.

Source: Exelixis, Inc.